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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,644	12/11/2000	Jean Gariepy	MMC.P-001	7797

21121 7590 08/10/2004

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,644	GARIEPY ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,24,25 and 27-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18, 20, and 24, 25, 27-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-18, 20, and 24, 25, 27-41 are pending.

Election/Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-16, drawn to a method for making a cytotoxic mutant protein.

Group II, claim(s) 17, drawn to a method of killing or inhibiting a target cell.

Group III, claim(s) 18, drawn to a method for identifying therapeutic protein.

Group IV, claim(s) 20, 27, 28, 29, drawn to a method for constructing a diagnostic probe.

Group V, claim(s) 24 and 25, drawn to a method for treating a condition.

Group VI, claim(s) 30 and 31, drawn to a composition comprising a cytotoxic mutated heteromeric protein of Shiga toxin or Shiga-like toxin.

Group VII, claim(s) 32, and 33, drawn to a method for making a medicament.

Group VIII, claim(s) 34-36, drawn to a combinatorial library comprising a plurality of microorganism clones expressing a plurality of variant forms of a protein toxin.

Group IX, claim(s) 37-41, drawn to a method for making a nucleic acid sequence encoding a cytotoxic mutant protein.

The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking groups I-IX appears to be that they all relate to a method of making a cytotoxic mutant protein having a mutated binding subunit by screening mutant variant forms of the protein against cells.

However, Jackson et al., *J. Bacteriol.* 172: 653-658 (1990) and Perera et al., *J. Bacteriol.* 173: 1151-1160 (1991) teach methods of making a cytotoxic mutant protein that is Shiga toxin and Shiga-like toxin, having a mutated binding B subunit by screening mutant variant forms of the protein against Vero and HeLa cells. Smedley et al., *Microbiology* 142: 1617-1624 (1996), teach methods of making a cytotoxic mutant protein that is *Bacillus thuringiensis* endotoxin, having a mutated binding B subunit by screening mutant variant forms of the protein against insect cells.

There is no special technical feature linking the claims and because the methods of groups I-IV, VI and VIII have different functions and different steps to carrying out those functions, unity of invention does not exist between groups I-IV, VI and VIII. Furthermore, the references of Jackson et al. and Perera et al. teach the composition comprising a cytotoxic mutated heteromeric protein of Shiga toxin or Shiga-like toxin of Group VI. Jackson et al., Perera et al. and Smedley et al. teach libraries comprising a plurality of microorganism clones expressing a plurality of variant forms of a heteromeric protein toxin.

It is noted that Claim 1 recites the language "screening cells which are substantially insensitive to the cytotoxic wild type protein"; this language, particularly "cells which are substantially insensitive" is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree of insensitivity of the cells. Thus one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention. Furthermore, while the specifications at, e.g., p. 20, lines 4-5 states that SK-BR-3 cell is a cell line that is "insensitive" to the wild-type toxin, the specification at p. 23, lines 24-25, states that the "susceptibility" of SK-BR-3 cells vary as a function of cell passage. Thus the claims and the specification do not provide a standard for determining whether a cell line is "substantially insensitive", for example, in terms of toxin concentration, percent survival or cell line passage number.

Also, the language "substantially insensitive" is not found in the specification as filed, but was introduced with the preliminary amendment, filed 8/4/2000. It is noted that the International Preliminary Examination Report, (hereinafter "IPER"), at Item I, states that amendments filed 04.05.00 "introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b)PCT." These amendments concerned claim 1, lines 1-3. The IPER stated that "[n]o basis for these amendments can be found in the application as filed." The IPER then stated that "Consequently, this report has been established as if said amendments had not been made (Rule 70.2(c)PCT), i.e. has been established on the basis of claims 1-26 as originally filed."

Accordingly, the groups are not linked by the same or a corresponding special technical feature as to form a single general inventive concept.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

A) Species where the screening cells that are bacteria, yeast, or tumors cells. Applicant must elect one, e.g., bacteria.

B) Species where the heteromeric protein toxin is Shiga toxin and Shiga-like toxin, ricin, abrin, gelonin, crotin, pokeweed antiviral protein, saporin, momordin, modeccin, sarcin, diphtheria toxin or Pseudomonas aeruginosa exotoxin A. Applicant must elect one, e.g., Shiga toxin and Shiga-like toxin.

C) Species where the binding subunit is of Shiga toxin and Shiga-like toxins, enterotoxins, cholera toxin, pertussis toxin or receptor binding domain of ricin. Applicant must elect one, e.g., Shiga toxin and Shiga-like toxin.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. **The reply must also identify the claims readable on the elected species, including any claims subsequently added.** An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

Claims 3, 4, 13 and 39 correspond to A) the species of screening cells.

Claim 9 corresponds to B) the species of heteromeric protein toxin.

Claim 16, 35 and 41 correspond to C) the species of binding subunits.

The following claim(s) are generic: Claims 1, 2, 8, 34, 37 and 38.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Jackson et al., *J. Bacteriol.* 172: 653-658 (1990) and Perera et al., *J. Bacteriol.* 173: 1151-1160 (1991) teach methods of making a cytotoxic mutant protein that is Shiga toxin and Shiga-like toxin, having a mutated binding B subunit by screening mutant variant forms of the protein against Vero and HeLa cells. Smedley et al., *Microbiology* 142: 1617-1624 (1996), teach methods of making a cytotoxic mutant protein that is *Bacillus thuringiensis* endotoxin, having a mutated binding B subunit by screening mutant variant forms of the protein against insect cells. Jackson et al. and Perera et al. teach the composition comprising a cytotoxic mutated heteromeric protein of Shiga toxin or Shiga-like toxin of Group VI and Jackson et al., Perera et al. and Smedley et al. teach combinatorial libraries comprising a plurality of microorganism clones expressing a plurality of variant forms of a heteromeric protein toxin.

Accordingly, the species are not linked by the same or a corresponding special technical feature as to form a single general inventive concept.

4. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER